UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/803,778	03/12/2001	Bridget Kathleen Mapleson	1324.024A	9665

23405 7590 07/07/2003

HESLIN ROTHENBERG FARLEY & MESITI PC
5 COLUMBIA CIRCLE
ALBANY, NY 12203

EXAMINER
ZEMAN, ROBERT A

ART UNIT	PAPER NUMBER
1645	8

DATE MAILED: 07/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application N .	Applicant(s)	
	09/803,778	MAPLESON ET AL.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE f this communication appears on the c ver sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment and response filed on 5-5-2003 are acknowledged. Claims 1,5 and 11 have been amended. Claims 1-5 and 7-20 are pending and currently under examination.

Claim Rejections Withdrawn

The rejection of claim 1 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the phrase "ionic surfactant effective to dissociate the endotoxin from the amphiphilic..." is withdrawn in light of the amendment thereto.

The rejection of claim 5 under 35 U.S.C. 112, second paragraph, for having insufficient antecedent basis for the limitation "the antigen" in line 1 is withdrawn in light of the amendment thereto.

The rejection of claim 11 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "analogue" is withdrawn in light of the amendment thereto.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 1-4 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "vaccine substance" is maintained for reasons of record.

The rejection of claim 4 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "vaccine antigen" is maintained for reasons of record.

Applicant argues:

1. A vaccine comprises some "vaccine substances" that are antigenic i.e. the "vaccine antigens" as well as non-antigenic vaccine substances.

2. The vaccine may include other factors such as an adjuvant or a preservative.

Applicant's arguments have been fully considered and deemed non-persuasive. It is unclear what is encompassed by said terms. Based on Applicant's argument the reagents used in the claimed process would constitute a "vaccine substance" and hence renders the claim indefinite. Moreover, contrary to Applicant's assertion the term "vaccine antigen" would likely be interpreted as anything in the vaccine that is immunogenic and is not restricted to the "object of the vaccine". Since the components of said vaccine have not ~~be~~ been set forth in the claims both terms are considered vague and indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1-5 and 7-20 under 35 U.S.C. 103(a) as being unpatentable over Shanbrom (EP 0 083 999) in view of Shanbrom (U.S. Patent 4,315,919) is maintained for reasons of record.

Applicant argues:

1. Shanbrom ('919) only teaches the use of a non-ionic, surfactant (Triton X 100).
2. Shanbrom (EP) also teaches the depyrogenation of a solution using a non-ionic surfactant.
3. Shanbrom (EP) does not evaluate the resulting vaccine maintained its efficacy.
4. Neither reference addresses the issues of whether filtration following depyrogenation with an ionic surfactant would satisfactorily remove said surfactant form the amphiphilic pharmaceutical drug or vaccine substance.
5. Neither reference alone or in combination contain the proper motivation for one of skill in the art to use an ionic surfactant to remove pyrogen from an amphiphilic drug or vaccine followed by filtration to remove the ionic surfactant with any assurance that the ionic surfactant has been satisfactorily removed from the pharmaceutical drug vaccine substance.

6. Even in combination, said references do not achieve the instant invention. Shanbrom (EP) does not disclose use of an ionic surfactant and Shanbrom ('919) fails to disclose the use of ultrafiltration as a means of separating the amphiphilic drug or vaccine from the ionic surfactant.

The instant claims are drawn to a method of removing bacterial endotoxin from a pharmaceutical process solution comprising treating the solution with an **ionic** surfactant effective to dissociate the endotoxin from the vaccine or pharmaceutical drug being purified and then filtering the solution through a molecular weight cut off filter having a pore size effective to retain said vaccine or pharmaceutical drug but allow the endotoxin to pass through. Said vaccine substance can be a polypeptide (claim 2), glycoprotein (claim 3) or a viral (influenza) antigen (claims 5, 7, 8 and 20). Said surfactant can be ionic, anionic (claim 9) or a bile salt [deoxycholate] (claims 10-13). Said cut off filter can be a regenerated cellulose acetate membrane or a polysulfone membrane (claim 17).

With regard to Points 1, 2, 5 and 6:

As outlined previously Shanbrom (EP 0 083 999) discloses a method of purifying biological, pharmaceutical and biomedical products comprising contacting said product with **a non-denaturing surfactant** (see pages 5-7). This encompasses **ionic** surfactants. Shanbrom further discloses the use of ultrafiltration techniques (including dialysis) to separate the biomedical product from surfactant and dissociated impurities (see page 10). Shanbron discloses that his method can be used for purifying both proteinaceous (see page 5) and non-proteinaceous (see page 7) products. Shanbrom differs from the claimed invention in that he does not explicitly

disclose the use of ionic surfactants such as deoxycholate or the use of filters comprising regenerated cellulose acetate membrane or a polysulfone membrane. Shanbrom (U.S. Patent 4,315,919) disclose a method of removing pyrogens (endotoxins) from biological and biomedical products utilizing a myriad of surfactants (see columns 1-5). Said surfactants include cationic, anionic, ampholytic and nonionic surfactants (see column 1, line 48 to column 2, line 50) Said surfactants also include salts of bile acids including sodium deoxycholate. Shanbrom further discloses that it might be necessary to separate the purified product from the surfactant and impurities (see column 3, line 67 to column 4, line 2). Consequently, it would have been obvious to one of ordinary skill in the art to utilize the various surfactants disclosed by Shanbrom (U.S. Patent 4,315,919) in the methods disclosed by Shanbrom (EP 0 083 999) since Shanbrom (EP 0 083 999) discloses the use of all non-denaturing surfactants (see page 5, lines 13-14) and Shanbrom (U.S. Patent 4,315,919) merely lists various non-denaturing surfactants. It should be noted that neither Shanbrom reference explicitly disclose the use of filters comprising regenerated cellulose acetate membrane or a polysulfone membrane. However, Shanbrom (EP 0 083 999) disclose the parameters to be used in his ultrafiltration techniques and hence, the use of a regenerated cellulose acetate membrane or a polysulfone membrane constitutes obvious variants of the disclosed ultrafiltration technique. Finally, the surfactant concentrations recited in claims 14-16 are equally obvious since one of ordinary skill in the art would optimize disclosed methods.

In response to applicant's argument that the references fail to show certain features of applicant's invention (Point 3), it is noted that the features upon which applicant relies (i.e., the efficacy of the drug or vaccine is maintained) are not recited in the rejected claim(s). Although

the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicant's argument that the references fail to show certain features of applicant's invention (Points 4-6), it is noted that the features upon which applicant relies (i.e., the ionic surfactant is satisfactorily removed from the drug or vaccine) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 308-7991. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Robert A. Zeman
July 1, 2003

L. F. Smith
LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600